

CLAIMS

We claim:

1. Stabilized polypeptide particles comprising a polypeptide and a stabilizing agent selected from the group consisting of metal ions and sugars that are stable under acidic conditions at temperatures up to or exceeding physiological conditions, the polypeptide particles being formulated to exhibit an acidic reconstitution pH.
2. The polypeptide particles of claim 1, wherein the polypeptide particles comprise a polypeptide, a metal ion and a sugar that is stable at acidic pH at temperatures up to and exceeding physiological conditions.
3. The polypeptide particles of claim 1, wherein the stabilizing agent is selected from disaccharides and monosaccharides that are stable under acidic conditions at temperatures up to and exceeding physiological conditions.
4. The polypeptide particles of claim 3, wherein the stabilizing agent is selected from trehalose and methyl-mannopyranoside.
5. The polypeptide particles of claim 1, wherein the stabilizing agent comprises a stabilizing agent selected from disaccharides and monosaccharides that are stable under acidic conditions at temperatures up to and exceeding physiological conditions and the stabilizing agent is included in the polypeptide particles at a wt/wt ratio of stabilizing agent to polypeptide that ranges between about 0.1/1 to about 1/1.
6. The polypeptide particles of claim 1, wherein the stabilizing agent comprises a stabilizing agent selected from disaccharides and monosaccharides that are stable under acidic conditions at temperatures up to and exceeding physiological conditions and the stabilizing agent is included in the polypeptide particles at a wt/wt ratio of stabilizing agent to polypeptide that ranges between about 0.1/1 to about 0.5/1.

7. The polypeptide particles of claim 1, wherein the stabilizing agent comprises a stabilizing agent selected from disaccharides and monosaccharides that are stable under acidic conditions at temperatures up to and exceeding physiological conditions and the stabilizing agent is included in the polypeptide particles at a wt/wt ratio of stabilizing agent to polypeptide that ranges between about 0.1/1 to about 0.25/1.

8. The polypeptide particles of claim 1, wherein the stabilizing agent comprises a metal ion derived from a divalent metal ion salt.

9. The polypeptide particles of claim 1, wherein the stabilizing agent comprises a metal ion derived from a divalent metal ion salt selected from the group consisting of CaCl_2 , MgCl_2 , and ZnCl_2 .

10. The polypeptide particles of claim 1, wherein the stabilizing agent comprises a metal ion and the molar ratio of the stabilizing agent to the polypeptide included in the polypeptide particles ranges from about 1/1 to about 10/1.

11. The polypeptide particles of claim 1, wherein the stabilizing agent comprises a metal ion and the molar ratio of the stabilizing agent to the polypeptide included in the polypeptide particles ranges from about 2/1 to about 6/1.

12. The polypeptide particles of claim 1, wherein the stabilizing agent comprises a metal ion and the molar ratio of the stabilizing agent to the polypeptide included in the polypeptide particles is about 4/1.

13. The polypeptide particles of claim 1, wherein the polypeptide is selected from the pituitary adenylate cyclase polypeptide/glucagon superfamily.

14. The polypeptide particles of claim 1, wherein the polypeptide is selected from group consisting of pituitary adenylate cyclase polypeptides, glucagons, glucagons-like peptides,

growth hormone releasing factor, vasoactive intestinal polypeptide, peptide histidine methionine, secretin, and glucose-dependent insulinotropic polypeptide.

15. Stabilized polypeptide particles comprising a pituitary adenylate cyclase polypeptide and a stabilizing sugar selected from trehalose and methyl-mannopyranoside, wherein the wt/wt ratio of stabilizing sugar to pituitary adenylate cyclase polypeptide included in the polypeptide particles is about 0.55/1 and the polypeptide particles are formulated to exhibit an acidic reconstitution pH.

16. Stabilized polypeptide particles comprising a pituitary adenylate cyclase polypeptide and a stabilizing metal ion selected from Ca^{2+} , Mg^{2+} , and Zn^{2+} , wherein the molar ratio of metal ion to pituitary adenylate cyclase polypeptide included in the polypeptide particles is about 4/1 and the polypeptide particles are formulated to exhibit an acidic reconstitution pH.

17. Polypeptide particles comprising a polypeptide and two or more stabilizing agents selected from the group consisting of metal ions, surfactants, buffers, and sugars that are stable in near neutral pH environments at temperatures up to and exceeding physiological conditions, the polypeptide particles being formulated to exhibit a near neutral reconstitution pH.

18. The polypeptide particles of claim 18, wherein the polypeptide is selected from the pituitary adenylate cyclase polypeptide/glucagon superfamily.

19. The polypeptide particles of claim 18, wherein the polypeptide is selected from group consisting of pituitary adenylate cyclase polypeptides, glucagons, glucagons-like peptides, growth hormone releasing factor, vasoactive intestinal polypeptide, peptide histidine methionine, secretin, and glucose-dependent insulinotropic polypeptide.

20. The polypeptide particles of claim 18, wherein the polypeptide particles comprise a stabilizing sugar and a buffer selected from amino acid buffers, peptide buffers and inorganic buffers.

21. The polypeptide particles of claim 21, wherein the wt/wt ratio of stabilizing sugar to polypeptide ranges from about 0.25/1 to about 1/1.
22. The polypeptide particles of claim 18, wherein the polypeptide particles comprise a buffer selected from amino acid buffers and peptide buffers and a stabilizing metal ion.
23. The polypeptide particles of claim 23, wherein the molar ratio of metal ion to polypeptide ranges from about 2/1 to about 10/1.
24. The polypeptide particles of claim 18, wherein the polypeptide particles comprise a buffer selected from amino acid buffers and peptide buffers and a surfactant.
25. The polypeptide particles of claim 25, wherein the surfactant accounts for between about 0.02 wt% and about 0.2 wt% of the polypeptide particles.
26. The polypeptide particles of claim 18, wherein the polypeptide particles comprise a buffer selected from amino acid buffers and peptide buffers, a surfactant, a metal ion and a stabilizing sugar.
27. The polypeptide particles of claim 18, wherein the surfactant comprises sodium dedocyl sulfate.
28. The polypeptide particles of claim 25, wherein the surfactant comprises sodium dedocyl sulfate and accounts for between about 0.02 wt% and about 0.2 wt% of the polypeptide particles
29. The polypeptide particles of claim 18, wherein the polypeptide is a pituitary adenylate cyclase polypeptide and the polypeptide particles comprise a buffer selected from amino acid buffers and peptide buffers and one or more additional stabilizing agents selected from the group consisting of a stabilizing sugar included at a wt/wt ratio of stabilizing sugar to polypeptide that ranges from about 0.25/1 to about 1/1, a metal ion included at molar ratio of metal ion to

polypeptide that ranges from about 2/1 to about 10/1, and a surfactant that accounts for between about 0.02 wt% and about 0.2 wt% of the polypeptide particles.

30. Stabilized polypeptide particles comprising a polypeptide that is stable under acidic conditions, wherein the polypeptide particles are formulated to exhibit an acidic reconstitution pH.
31. The stabilized polypeptide particles of claim 30, wherein the stabilized polypeptide particles are formulated to exhibit a reconstitution pH below pH 5.
32. The stabilized polypeptide particles of claim 30, wherein the stabilized polypeptide particles are formulated to exhibit a reconstitution pH between about pH 2 and pH 4.
33. The stabilized polypeptide particles of claim 30, wherein the polypeptide comprises a polypeptide selected from the group consisting of pituitary adenylate cyclase polypeptides, glucagons, glucagons-like peptides, growth hormone releasing factor, vasoactive intestinal polypeptide, peptide histidine methionine, secretin, and glucose-dependent insulintropic polypeptide, and the particles are formulated to exhibit a reconstitution pH below pH 5.
34. The stabilized polypeptide particles of claim 30, wherein the polypeptide comprises a polypeptide selected from the group consisting of pituitary adenylate cyclase polypeptides, glucagons, glucagons-like peptides, growth hormone releasing factor, vasoactive intestinal polypeptide, peptide histidine methionine, secretin, and glucose-dependent insulintropic polypeptide, and the particles are formulated to exhibit a reconstitution pH between about pH 2 and pH 4.
35. The stabilized polypeptide particles of claim 30, wherein the polypeptide comprises a pituitary adenylate cyclase polypeptide analog and the particles are formulated to allow recovery of greater than 90% of the initial pituitary adenylate cyclase polypeptide analog and permit less than 2% dimer formation after two months of storage at 60° C.